Paper No. 48

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte DONALD B. KOHN, R. MICHAEL BLAESE, CRAIG A. MULLEN and ROBERT C. MOEN

Appeal No. 2004-0577
Application No. 08/225,478

ON BRIEF

Before WILLIAM F. SMITH, SCHEINER and GREEN, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1-3, 5, 21 and 22. Claims 4, 6-15 and 23-26 are also pending; claims 6-15 and 23-26 have been allowed; claim 4 has been objected to.

Claim 1 is representative of the subject matter on appeal:

1. A method of expressing a therapeutic agent in a human, comprising:

administering autologous CD34+ cells obtained from cord blood to said human, said autologous CD34+ cells having been genetically engineered to include at least one nucleic acid sequence encoding a therapeutic agent.

The references relied on by the examiner are:

Kohn et al. (Kohn), "Engraftment of Gene-Modified Umbilical Cord Blood Cells in Neonates with Adenosine Deaminase Deficiency," Nature Medicine, vol. 1, no. 10, pp. 1017-1023 (October 1995)

Orkin et al. (Orkin), "Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy" (December 7, 1995)

Claims 1-3, 5, 21 and 22 stand rejected under the first paragraph of 35 U.S.C. § 112, as based on a non-enabling disclosure. The Answer refers to paper no. 33 for the statement of the rejection; paper no. 33 refers, in turn, to paper no. 29.

We reverse the examiner's rejection.

BACKGROUND

"[T]his invention relates to gene therapy in a human patient by administering to the patient [autologous] CD34+ cells genetically engineered with at least one DNA sequence encoding a therapeutic agent . . . as an alternative to allogenic bone marrow transplantation." Specification, page 1. Umbilical cord blood "represent[s] a uniquely rich source of hematopoietic stem cells [ ]. Large numbers of stem cells can be collected from normal cord and placental blood without cytokine mobilization and without performing invasive procedures on the patient . . . Within two days of birth, the number of circulating hematopoietic progenitor cells drops dramatically to the level seen in older children and adults; thus, collection of stem cells at birth from the cord . . . represents a unique opportunity to obtain cells needed for gene therapy . . . easily and safely." Id., page 2. "[C]onditions which permit in vitro gene transfer into umbilical cord blood cells . . . [include] co-cultivation . . . viral supernatant transduction on a marrow stromal layer . . . and transduction with viral supernatant alone." Id., pages 2-3.

DISCUSSION

The claims are directed to a method of expressing a therapeutic agent in a human by administering transduced autologous CD34+ cells obtained from cord blood, wherein the transduced cells encode and express a therapeutic agent.

According to the examiner, the specification is "enabling for claims limited to methods of treating severe combined immunodeficiency [(SCID)] syndrome using therapeutic gene transfer to autologous CD34+ cell[s] obtained from cord blood cells wherein said cells have been genetically engineered with a nucleic acid encoding adenosine deaminase (ADA) . . . , [but] does not reasonably provide enablement for the treatment of any and all diseases with any and all . . . nucleic acids" (paper no. 33, page 2).

In reviewing the examiner's analysis in support of the rejection, it appears that his conclusion is based on two principle concerns. First, that the field of gene therapy is, and "remains plagued by an exceedingly high level of unpredictability" (paper no. 29, page 3); second, that the ADA gene is a special case, "by virtue of its favorable characteristics" (id.).

The examiner cites Kohn and Orkin in support of his assertion that "the field [was] so unpredictable that those of skill in the art could only use the ADA gene in the claimed methods to provide a therapeutic effect for the SCID condition as is evidenced by (1) the disclosure of support for ADA, and ADA alone, by virtue of its favorable characteristics and (2) the documented unpredictability in the art of gene therapy which would effectively hinder the skilled artisan from practicing the claimed invention without having to undertake undue experimentation using any given nucleic acid sequence" (paper no. 29, page 3).

In our view, the examiner's position does not reflect the applicable legal standard. In In re Brana, 51 F.3d 1560, 1567, 34 USPQ2d 1436, 1442 (Fed. Cir. 1995), the court cautioned against confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption," citing Scott v. Finney, 34 F3d 1058, 1063, 32 USPQ2d 1115, 1120 (Fed. Cir. 1994). The rejection before the court for review in Brana was for lack of enablement under the first paragraph of 35 U.S.C. § 112 (although the court discussed the issues raised in the appeal in the context of both enablement and the utility requirement of 35 U.S.C. § 101):

> On the basis of animal studies, and controlled testing in a limited number of humans (referred to as Phase I testing), the Food and Drug Administration may authorize Phase II clinical studies . . . The purpose of the Phase II study is to determine primarily the safety of the drug when administered to a larger human population, as well as its potential efficacy under different dosage regimes. [ ]
>
> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. [ ] Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana, 51 F3d at 1568, 34 USPQ2d at 1442-43 (citations omitted). The court also expressed its "firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, even though it may eventually appear that the compound is without value in the treatment of humans" (quoting In re Krimmel, 292 F.2d 948, 953, 130 USPQ 215, 219 (CCPA 1961)).

While the claims involved in Brana were directed to chemical compounds taught to be useful in treating cancer, we believe these principles can be applied to the present claims directed to methods of expressing therapeutic agents in humans using transduced autologous CD34+ cells from cord blood.

The references relied on by the examiner support his position that the future course of gene therapy was uncertain at the time the present application was filed. Nevertheless, these same references provide evidence that the field had reached that stage of "[u]sefulness in patent law" described in Brana. For example, Orkin acknowledges that "[s]ignificant problems remain in all basic aspects of gene therapy . . . includ[ing] shortcomings in all current gene transfer vectors and an inadequate understanding of the biological interaction of these vectors with th host," but nevertheless notes that over a hundred clinical gene therapy protocols have been reviewed and approved, and maintains that "[c]linical studies represent [ ] practical implementation of basic discoveries," thus, "[t]here is a clear and legitimate need for clinical studies to evaluate various aspects of gene therapy approaches" (Orkin, pages 1 and 2, and Table 3).

Again, we note that the claims are directed to a method of expressing a therapeutic agent in a human by administering transduced autologous CD34+ cells obtained from cord blood. The examiner acknowledges that appellants have demonstrated expression of ADA in human infants reconstituted with transduced autologous CD34+ cells obtained from cord blood (see e.g., paper no. 29, page 6) - in our view, a stage at which an invention in this field is useful.

Moreover,

> [A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). Additionally,

> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

Id. at 224, 169 USPQ at 370. Here, the examiner has not explained why one skilled in the art would not have expected other genes to be similarly expressed - only that, ultimately, a therapeutic benefit may not be obtained "[i]f the therapeutic agent is recognized by the body as 'foreign,' [if] the transfected cells [are] eliminated by the immune system[,] [i]f expression of the inserted DNA rapidly declines[,]" etc. Answer, page 4.

Our review of the examiner's evidence in light of the standard for enablement and/or utility articulated in Brana leads us to conclude that the evidence does not support the broad proposition that gene therapy is nonenabled. Moreover, we find that the examiner has not established that appellants' specification is not enabling for expressing therapeutic agents (other than ADA) in humans by administering transduced autologous CD34+ cells obtained from cord blood.

On this record, we hold that the examiner has failed to establish that the claimed subject matter is non-enabled. Accordingly, the rejection of claims 1-3, 5, 21 and 22 under the first paragraph of 35 U.S.C. § 112 is reversed.

REVERSED

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